ADAA: A Morphology-Aware Method for Local Activation Time Computation using Cross Correlation

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Abstract

Accurate estimation of activation times is crucial in electrophysiological studies to assess depolarization wave propagation direction. Rule-based methods, such as the Steepest Deflection (SD) method, have been prevalent, but their lack of robustness is a major limitation, leading to exploring alternative methodologies. The Directional Activation Algorithm (DDA) [1, 2] leverages delays between electrogram (EGM) signals. We generalize the DAA framework by utilizing cross-correlation analysis to compute pairwise relative delays between EGMs. Our Adaptive Direction Activation Algorithm (ADAA) integrates morphological characteristics and initial activation time estimates to enhance accuracy and robustness. Our contribution lies in the introduction of a more robust and general model that can be fitted with the same computational cost as DAA. We formulate the optimization problem and derive a closed-form solution. Through evaluation on both toy model data and realistic simulations, we demonstrated the superior efficacy of our methodology in estimating activation times compared to existing methods. In specific settings, our approach reduces the mean squared error (MSE) by 50%.

1. Introduction

Cardiac arrhythmias such as fibrillation and tachycardia (atrial or ventricular) are common cardiac arrhythmias which are associated with a high overall risk of mortality. In some cases it is necessary to perform an interventional procedure, during which intracardiac EGMs are recorded. In the literature, researchers often investigate the mechanisms underlying the pathology and use the electrocardiograms to provide insights into the propagation patterns of depolarization wave-fronts in the heart, potentially detecting pathological substrates related to arrhythmias. A central point to understanding cardiac activation dynamics is the accurate determination of local activation times (LATs), marking the moment when depolarization reaches specific electrodes. While conventional LATs estimation methods are rule-based, they are not robust to some noise and interference, especially when dealing with bipolar electrograms. To address these limitations, researchers have explored alternative techniques, including wavelets decomposition [3] or cross-correlation analysis [1]. More details and other methods can be found in the Cantwell et al. survey [4].

In this work, we focus on the application of cross-correlation for LAT estimation, aiming to refine existing methodologies like the ones proposed in [1] or [5]. The initial method (DAA) described in [1] focused only on adjacent electrodes to compute the cross correlation, then deriving the absolute activation times from the delays. Then, by conceptualizing the electrode array as a graph, Kölling et al. [5] generalized this method considering electrode pairs with varying distances, expanding the scope of analysis. While these methods show great results compared to standard rule-based methods, two limitations can be identified. First, the activation times remain relative since the smaller activation time is set to 0, and this can be an issue when merging several outputs of the method as we lose the chronology between the two sets of electrograms. Secondly, cross-correlation-based delays estimation can be difficult when dealing with signals with varied morphology, leading to misleading results. This issue is often met when dealing with pathological tissues because of the presence of highly fragmented signals.

Contributions: In this paper, we propose to generalize the DAA method to address the limitations of getting a relative activation time and being sensible to the signal morphology variability. We propose a hybrid method based on the same methodology than the one in [1] and [5], but leveraging a first estimation of the LAT (using rule-based method for example) and weighing the optimization problem based on the signals similarities (cf Figure 1). We validate our method through evaluation on both synthetic and simulated data, and we assess the efficacy of our approach compared to the rule-based methods, and to the global methods introduced in [1] and [5].

2. Methods

2.1. Preliminaries

Given N electrograms $X_1[1 : T], ..., X_N[1 : T]$ recorded at several locations and their respective activation times $\tau = [\tau_1, ..., \tau_N] \in \{1, ..., T\}^N$, the objective is to retrieve τ from the signals.
In [1], the authors introduce a global method based on cross-correlation allowing to compute the activation times from a multivariate perspective.
Let $x, y : \mathbb{Z} \to \mathbb{R}$ be two time series with a finite support. The cross-correlation $C_{x,y} : \mathbb{Z} \to \mathbb{R}$ between x and y is defined by:

$$C_{x,y}[i] = \frac{\sum_k x[k]y[k-i]}{\left(\sum_k x[k]^2\right)\left(\sum_k y[k]^2\right)} \quad , \quad i \in \mathbb{Z} \tag{1}$$

The delay between x and y is then defined as:

$$\delta_{x,y} = arg \max_i |C_{x,y}[i]| \tag{2}$$

Given pairwise delays $(\delta_{i,j})_{1 \le i < j \le N}$ between $X_1, ..., X_N$, the method in [1] computes the activation times $\hat{\tau}$ minimizing the errors with the delays in the least square sense:

$$\min_{\hat{\tau}_1,...,\hat{\tau}_N} \sum_{1 \le i < j \le N} (\hat{\tau}_i - \hat{\tau}_j - \delta_{i,j})^2 \tag{3}$$

Such an optimization problem corresponds to a linear problem under Gaussian assumption:

$$\begin{bmatrix} \delta_{1,2} \\ \delta_{1,3} \\ \vdots \\ \delta_{i,j} \\ \vdots \end{bmatrix} = \begin{bmatrix} \hat{\tau}_2 - \hat{\tau}_1 \\ \hat{\tau}_3 - \hat{\tau}_1 \\ \vdots \\ \hat{\tau}_j - \hat{\tau}_i \\ \vdots \end{bmatrix} + \begin{bmatrix} \varepsilon_{1,2} \\ \varepsilon_{1,3} \\ \vdots \\ \varepsilon_{i,j} \\ \vdots \end{bmatrix}$$

where $\epsilon_{i,j} \sim \mathcal{N}(0, 1)$ for all $1 \le i < j \le N$.
In vector form we can write the problem as:

$$\mathbf{d} = \mathbf{B}^T \hat{\tau} + \varepsilon \tag{4}$$

where

$$\mathbf{B}^T = \begin{bmatrix} -1 & 1 & 0 & 0 & \dots & 0 & \dots & 0 \\ -1 & 0 & 1 & 0 & \dots & 0 & \dots & 0 \\ \vdots & \vdots & \vdots & \vdots & & \vdots & & \vdots \\ 0 & -1 & 1 & 0 & \dots & 0 & \dots & 0 \\ \vdots & \vdots & \vdots & \vdots & & \vdots & & \vdots \\ 0 & 0 & 0 & 0 & \dots & -1 & \dots & 1 \end{bmatrix}.$$

The solution $\hat{\tau}$ satisfies

$$\mathbf{B}\mathbf{B}^{\mathbf{T}}\hat{\tau} = \mathbf{B}\mathbf{d}.$$

In [5], the authors propose to add or remove some rows and columns in the matrix $\mathbf{B}^{\mathbf{T}}$ selecting neighbors from 1 hop to p hops away in the graph. They concluded that the higher p the better the results.

2.2. Method formulation

While in [5] the authors propose to leverage a binary graph incidence matrix to take into account more or less number of hops in the optimization problem, we introduce here a generalized model dealing with a weighted graph.
Let $\mathcal{G} = (\mathcal{V}, \mathcal{E})$ an undirected graph with vertices $\mathcal{V} = \{1, ..., N\}$ and $\mathcal{E} = \{((i,j), w_{i,j})\}_{1 \le i < j \le N}$ the weighted edges. We propose to solve the following generalized problem:

$$\min_{\hat{\tau}_1,...,\hat{\tau}_N} \sum_{1 \le i < j \le N} w_{i,j} \left(\hat{\tau}_i - \hat{\tau}_j - \delta_{i,j}\right)^2, \tag{5}$$

where $\mathbf{w} = [w_{i,j}]_{1 \le i < j \le N}$ are positive weights encoding the activation patterns similarities. They are given by $w_{i,j} = T_l\left(\max_k |C_{X_i,X_j}[k]|\right)$, where T_l is the thresholding application defined by $T_l(x) = \begin{cases} 0 \text{ if } x < l \\ x \text{ otherwise} \end{cases}$.
Note that there is no additional computation since it is already done to compute the pairwise delays. Thus this generalized version has the same computational cost as the DAA.
Let $\mathbf{W} = diag\left([w_{1,1}, ..., w_{1,N}, w_{2,3}, ..., w_{N-1,N}]\right)$, in vector form the problem becomes:

$$\min_{\hat{\tau}_1,...,\hat{\tau}_N} \left|\left|\mathbf{B}^{\mathbf{T}}\hat{\tau} - \mathbf{d}\right|\right|^2_{\mathbf{W}}, \tag{6}$$

where $\left|\left|\mathbf{B}^{\mathbf{T}}\hat{\tau} - \mathbf{d}\right|\right|^2_{\mathbf{W}}$ denotes $\left(\mathbf{B}^{\mathbf{T}}\hat{\tau} - \mathbf{d}\right)^T \mathbf{W} \left(\mathbf{B}^{\mathbf{T}}\hat{\tau} - \mathbf{d}\right)$.
Then, to address the issue of obtaining absolute activation times, and be able to solve the problem with a disconnected graph, we propose to leverage a first estimation

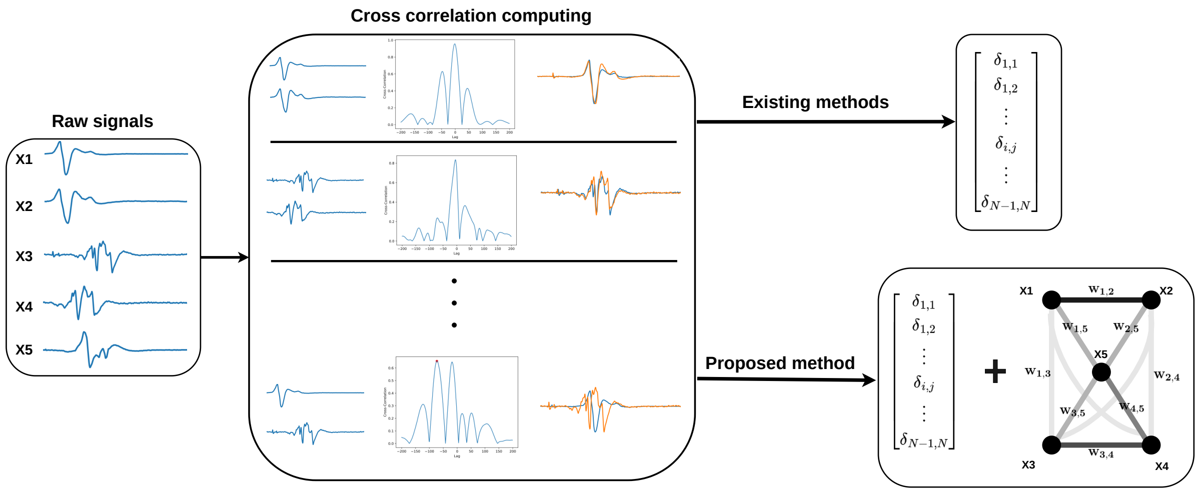

Figure 1. Illustration of the proposed framework compared to the DAA method.

of the activation times by assuming that this estimator follows a normal distribution centered in the true activation time: $\tilde{\tau} \sim \mathcal{N}(\tau, \sigma^2 I_d)$. In practice, we can for example use a rule-based method (cf [4] for a survey of the existing methods).
Finally, the problems becomes:

$$\min_{\hat{\tau}_1,\ldots,\hat{\tau}_N} ||\mathbf{B^T}\hat{\tau} - \mathbf{d}||^2_{\mathbf{W}} + \lambda||\hat{\tau} - \tilde{\tau}||_2^2, \tag{7}$$

with $\lambda = \frac{1}{2\sigma^2}$ is an hyper-parameter. Note that the larger λ, the higher the confidence in the first estimation.
This optimization problem has a closed-form solution and it is given by:

$$\hat{\tau} = \left(\mathbf{BWB^T} + \lambda\mathbf{Id}\right)^{-1}(\mathbf{BWd} + \lambda\tilde{\tau}). \tag{8}$$

3. Results

In this section, we present the results achieved with a toy model dataset and simulated data are presented. We compare ADAA, DAA (version in [5]) and a rule-based method ($\max \frac{dV}{dt}$).

Toy dataset.
The aim of our method is to generalize the ones in [1, 5] so as to deal with signals with several morphology. To illustrate this idea, we created synthetic datasets using 4 patterns (one healthy and three with fractionation). We construct the N signals by choosing randomly one of the four patterns, applying a temporal shift and adding some Gaussian noise. The first LAT estimations $\tilde{\tau}$ were taken as a uniform random variable in $[\![\tau - 10, \tau + 10]\!]$ where τ is the true LAT. We tested several settings by taking $N \in \{10, 30, 50\}$ and checking the methods with datasets built using a range from 1 pattern to 4 patterns to understand whether our method is able to compute LATs with a high morphology variability. To compare the two methods we used the Mean Squared Error (MSE) defined by:

$$\text{MSE}(\hat{\tau}, \tau) = \frac{1}{N}\sum_{i=1}^{N}(\hat{\tau}_i - \tau_i)^2. \tag{9}$$

We ran experiments 50 times for each settings. The results are presented in Figure 2 (a) and (b) and we observe that when more than 3 different patterns are present in the EGMs, Adaptive DAA outperforms DAA, dividing the MSE by 3 for 3 patterns and by 2 for 4 patterns. Moreover, the results show that while adding more EGMs does not change the results obtained by DAA (MSE is around 3.5 from 10 to 50 EGMs), the Adaptive DAA appears to perform better as the dimension increases (from 2.5 with 10 EGMs to 1.5 for 50 EGMs).

Simulated Electrograms
In this section, we run experiments with simulated electrograms. To simulate data, we followed the model proposed in [6], which is used in several works (including [5,7]). The tissue is discretized on a two-dimensional grid, and the electrical propagation from cell to cell is governed by a reaction-diffusion equation. We then simulate the electrode recording by computing the convolution over the space of the transmembrane currents, making sure the resulting EGMs were coherent after visual inspection. Simulated data were generated by adding line blocks and slowing area and we compare our method with DAA and a rule-based method ($\max dV/dt$). Note that here $\tilde{\tau}$ is taken as

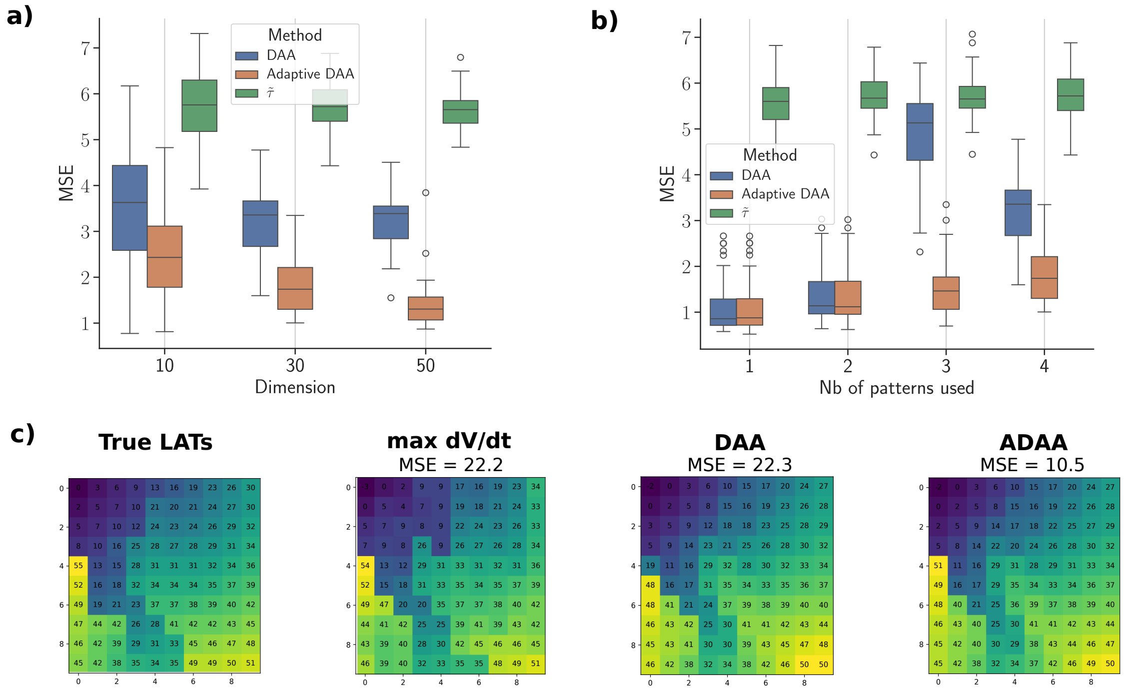

Figure 2. **a)** MSE plotting against the number of EGMs considered. Experiments were run on data built using the 4 patterns. **b)** MSE plotting against the number of patterns used to create the data. We considered 30 EGMs for each experiment. **c)** Results obtained with the simulated data.

the LAT computed by the rule-based method.
The results are featured in Figure 2 and show better results with Adaptive DAA. The MSE is halved compared to DAA or the rule-based method and the global propagation pattern resulting of Adaptive DAA seems to be more realistic than the others.

4. Conclusion

We presented a generalized version of DAA [1], called Adaptive DAA, which relies on an additional weighted regularization approach depending on the correlation between signals with the same computational cost as the orignal method (DAA). We derived the closed form of the solution and conducted experiments with synthetic data showing better quantitative results than DAA or rule-based methods. Tests conducted with real data hold significant interest and are envisioned for exploration in subsequent works.

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